

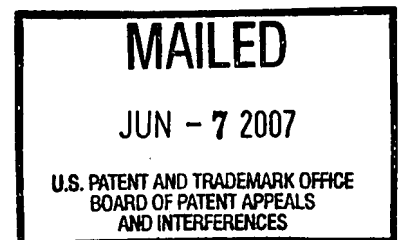
1 RECORD OF ORAL HEARING
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3 UNITED STATES PATENT AND TRADEMARK OFFICE
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6 BEFORE THE BOARD OF PATENT APPEALS
7 AND INTERFERENCES
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10 Ex parte JOOST VAN NEERVEN
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13 Appeal 2007-1070
14 Application 09/467,901
15 Technology Center 1600
16

17
18 Oral Hearing Held: April 24, 2007
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22 Before DONALD E. ADAMS, DEMETRA J. MILLS, and
23 RICHARD M. LEBOVITZ, Administrative Patent Judges
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26 On Behalf of the Appellant:
27

28 MARYANN T. PUGLIELLI, ESQ.
29 Finnegan, Henderson, et al.
30 901 New York Avenue, NW
31 Washington, D.C. 20001-4413
32 202/408-6054
33

34 The above-entitled matter came on for hearing on Tuesday, April 24,
35 2007, commencing at 2:30 p.m., at The U.S. Patent and Trademark Office,
36 600 Dulany Street, 9th Floor, Alexandria, Virginia, before Jan M. Jablonsky,
37 Notary Public.

1 CLERK: Calendar Number 24, Appeal number 20071070. Maryann
2 Puglielli.

3 JUDGE ADAMS: Thank you. Good afternoon.

4 MS. PUGLIELLI: Good afternoon. How are you?

5 JUDGE ADAMS: Very good. How are you?

6 MS. PUGLIELLI: Good.

7 JUDGE ADAMS: Would you like to introduce your associate?

8 MS. PUGLIELLI: Excuse me?

9 JUDGE ADAMS: Introduce your associate?

10 MS. PUGLIELLI: Yes.

11 JUDGE ADAMS: And we're familiar with your issues and
12 once you introduce your associate, you have 20 minutes.

13 MS. PUGLIELLI: Okay, great. Thank you. This is Andy
14 Holtman.

15 JUDGE ADAMS: Greetings.

16 MS. PUGLIELLI: And what I would like to do -- so what I
17 would like to do, if it please the Court, your Honors, is begin with an
18 explanation of the most important parts of the invention. And because of
19 those most important parts, I'd also like to provide you with a very short
20 explanation of what the functions of IgE are as an antibody. And then
21 conclude by going through the references and explaining how it is that we
22 believe that the references are quite different from the invention.

23 So may I proceed with that, or --

24 JUDGE ADAMS: Quickly. I think we're pretty familiar with
25 the function of IgE and the context of the claimed invention. So if you want
26 to quickly go through that, that would be great.

1 MS. PUGLIELLI: Okay.

2 The invention unlike other more standard assays is seeking to
3 provide very important information about exactly what is going on with the
4 allergic immune response. And let me just interject that if, at any point, you
5 want to ask questions about what I'm discussing, please feel free to stop me.

6 Other assays that don't employ receptors are not going to
7 provide this information. Because in vivo, IgE exerts its function as part of
8 the allergic response by bonding to the receptor on the cells and then the
9 cells in turn activate.

10 The other thing that the invention seeks to do that the references
11 are not approaching is trying to preserve the types of in vivo interactions that
12 happen with IgE antibody and its receptors. And also trying to preserve
13 those interfering interactions that can happen in vivo, so it may not
14 necessarily be a clean interaction between the antibody and its receptor.

15 Now, with that said, of course, IgE exerts its function through
16 two different receptors, a high-affinity receptor and a low-affinity receptor.
17 And the high-affinity receptor is expressed on a certain group of cells and
18 the low-affinity receptor is expressed in a certain group of cells. And
19 depending on which cell that receptor is attached to, you will get a different
20 reaction. So it's a very general, very quick example.

21 For the high-affinity receptor, which is really involved in rapid
22 allergic responses, like anaphylaxis, for example, you can have histamine
23 production, you can have IL10 production, you can have nerve growth factor
24 production. And again the issue is not so much exactly what do these things
25 do, but that you get a certain profile of -- of the cascade of events that is
26 going to happen because of which receptor is involved.

1 In contrast, the low-affinity receptor, which deals more so with
2 the long-term allergic response, can also do things like trigger histamine
3 production, but it also can deal with cell migration. So inviting other cells to
4 come to the site of the allergic response. It can also deal with antigen
5 transport so that more antigen is transported, for example, through an
6 intestinal wall and thereby enhancing the allergic response.

7 So when you think about the cellular events going on with the
8 high-affinity receptor versus low-affinity receptor, they are very different
9 things.

10 Now, going back to the invention, because the invention is
11 using these receptors, and the claims invoke not only the potential usage of
12 both receptors at the same time, but also the use of one receptor and then
13 separately from the other receptor, it's going to provide the physician with an
14 idea of what kind of allergic response is that patient prone to make.

15 JUDGE LEBOVITZ: But because the claim says and/or, it
16 covers essentially three different embodiments, and all we have to find one
17 embodiment obvious, because that's enough to make a claim unpatentable.

18 MS. PUGLIELLI: So with that said, again, a reference like, for
19 example, Johansen, which is using an antibody in order to do the detecting
20 of the IgE complex instead of using a receptor, is not going to be able to
21 provide that kind of information.

22 JUDGE LEBOVITZ: Why not? What can't it provide?
23 Because the Johansen reference was using anti-IgE directed against the FC.
24 The claimed invention uses receptors. How -- FC1 or FC2. How is that
25 interaction different? And what evidence do you have of the difference that

1 you get a different result when you use the FC1 or 2 to pull down an IgE
2 versus using the anti-IgE to pull down an IgE complex?

3 MS. PUGLIELLI: Well, for example, in the Frank reference,
4 and this was something that the examiner had brought out in the prosecution,
5 in the Frank reference, the reference was discussing how an IgE receptor can
6 have less cross-reactivity than using simply an antibody that's binding to an
7 IgE molecule. How the receptor can have higher sensitivity. So those types
8 of facts, in terms of comparing the receptor versus the antibody, showed that
9 the two really are not equivalent reagents, simply because they both have the
10 propensity to bind IgE.

11 JUDGE ADAMS: So by combining Johansen and Frank, Frank
12 actually motivates one to use an FC receptor rather than an antibody bound
13 to the support structure?

14 MS. PUGLIELLI: Well, if the -- if the artisan were to read
15 Frank and take that supposed teaching --

16 JUDGE ADAMS: The teaching you just relied upon, right?

17 MS. PUGLIELLI: Right.

18 JUDGE ADAMS: Okay.

19 MS. PUGLIELLI: And take that teaching and look at
20 Johansen, Johansen uses an anti -- as you're saying -- uses an anti-FC IgE
21 antibody. And so if Frank is teaching away from using that type of antibody
22 and then the artisan looks at Johansen, which does exactly what Frank is
23 telling you not to do, then there wouldn't be that motivation to combine them
24 and say, oh, well, I should put a receptor in.

25 Frank really provides a laundry list of different types of
26 reagents that you could use in the assays and it doesn't highlight any one of

1 them as being particularly beneficial over any other. Not only does it
2 discuss potentially hundreds of thousands of different combinations of assay
3 reagents, it also talks about and lists as a laundry list, you could do it in this
4 format, that format, this format, that format.

5 JUDGE ADAMS: Other than the IgE FC, what does Frank
6 teach for that particular binder for that particular IgE to this molecule?

7 MS. PUGLIELLI: Well, the thrust of Frank is that it's -- it
8 focuses on the discovery, really, of the canine version of the high-affinity
9 receptor. And most of the examples in Frank deal with how did we clone it,
10 how do you express it? And then the description section of the reference
11 really goes into well, here are a bunch of different assay formats, different
12 ways in which you could do it, and you could use this canine receptor in
13 those assay formats. But again --

14 JUDGE ADAMS: So notwithstanding all the other reagents
15 that he might use in his -- in his assay, he talks about using the Fcε, right?

16 MS. PUGLIELLI: He talks about using the --

17 JUDGE ADAMS: Does he talk about any other molecule other
18 than Fcε?

19 MS. PUGLIELLI: I'm sorry, could you say that again?

20 JUDGE ADAMS: Does he -- does he talk about any other
21 molecule other than the Fcε receptor?

22 MS. PUGLIELLI: There are some embodiments in which he is
23 just using the receptor alone to detect the presence of an antibody. There are
24 some embodiments where he's trying to invoke the presence of a ligand as
25 well.

1 Even in the situations where you think of all three of those
2 components, again the way in which Frank discusses --

3 JUDGE ADAMS: Let's be clear. All three of which
4 components?

5 MS. PUGLIELLI: A ligand, an IgE antibody and the canine
6 receptor.

7 JUDGE LEOVITZ: Can we just clarify, we're talking about
8 Frank?

9 MS. PUGLIELLI: Yes, Frank.

10 JUDGE LEOVITZ: And Frank is talking about the Fcε
11 receptor?

12 MS. PUGLIELLI: Canine, yes. Yes.

13 JUDGE LEOVITZ: But the claims which the examiner
14 pointed out were not limited to human or any species or even mammalian.
15 They just say, Fcε --

16 MS. PUGLIELLI: -- receptor.

17 JUDGE LEOVITZ: Right.

18 MS. PUGLIELLI: To go back to your question about also why
19 is it important to use the receptor as opposed to an antibody, for example,
20 Figure 2 is justification. Which, if you don't have that before you, I can give
21 you copies.

22 JUDGE ADAMS: No, we have it.

23 MS. PUGLIELLI: All three of you have it?

24 JUDGE ADAMS: The spec? Figure 2 of the specification?

25 JUDGE LEOVITZ: Yeah, we have it.

1 MS. PUGLIELLI: So that provides actually a beautiful
2 example of how an antibody detection, or an antibody mediated detection is
3 going to differ from what a receptor can do.

4 JUDGE LEOVITZ: Can you refer again to where you're
5 talking about?

6 MS. PUGLIELLI: Figure 2.

7 JUDGE LEOVITZ: Figure 2. Thanks. Sorry.

8 MS. PUGLIELLI: Figure 2. So looking at Figure 2, and I'll try
9 to do this as quickly as possible, because your time is very precious.

10 In Figure 2, Figure 2 is using the assay of the invention. It's
11 using B-cells that are expressing the CD23 receptor. And just to very
12 quickly take you through each of these columns, that is if you're holding the
13 -- if you're holding the table on its side so you can actually read what the
14 axes say, the very top column is really a negative control, where you're
15 taking serum from an allergic patient and you're not adding any allergen
16 whatsoever. And so you expect that there is not going to be an interaction,
17 because the interaction between IgE and the receptor is going to have to
18 involve the ligand as well.

19 Now, the -- the next one is really a positive control, taking the
20 allergic serum and then exposing to it the ligand that it's going to bind to,
21 and then you've got the receptors. And of course, you see plenty of
22 fluorescence coming out.

23 Then in the next sample, you're taking the allergic patient's
24 serum and you're adding to it serum from a person who has undergone SAB
25 treatment, which is a process of desensitizing a patient to an allergen that

1 they're allergic to. And you add the allergen. And you see that significantly
2 the amount of fluorescence goes down there.

3 And then as another control, they have at the end SAB treated
4 serum along with allergen.

5 Now, if you look at Figure 2.B, they are the same samples as
6 I've just described them, except Figure 2.B is using an assay in which you
7 are using an antibody to detect the complex. And what's of most importance
8 is if you go to the third column or the third line, if you will, of Figure 2.B,
9 you see that in that sample with the allergic patient serum, with the SAB
10 treated serum and the allergen, there's still plenty of IgE there, that this
11 antibody is detecting.

12 However, when it comes down to actually determining how
13 much of that IgE is going to be participating in an immune reaction or an
14 immune response, it's quite a different picture, that only the invention is
15 going to show the physician, because the invention is using a receptor to
16 detect the presence of these complexes, as normally would be in vivo, as
17 opposed to using an antibody.

18 JUDGE ADAMS: Isn't that exactly what Frank says is the
19 problem with using antibodies in this type of assay?

20 MS. PUGLIELLI: But again, Frank is only providing a very
21 large laundry list --

22 JUDGE ADAMS: We had that discussion about reagents. And
23 you were unable to tell me what, other than Fce Franks taught to bind its
24 antibody. All right, so there might be a whole laundry list of other agents
25 that are possibly involved in these reagents. But what is it, I'll ask you one

1 last time, what is it other than Fcε receptor is Franks using to bind its
2 antibody?

3 MS. PUGLIELLI: Well, the type of teaching of higher
4 sensitivity and higher specificity is going towards the direction of trying to
5 detect as much IgE as you possibly can, as opposed to being concerned with
6 mimicking these interactions.

7 JUDGE ADAMS: Like nonspecific -- doesn't he talk about
8 nonspecific binding?

9 JUDGE LEOVITZ: Can I -- there are two kinds of assays
10 that are being done. One is an assay that detects total IgE and another assay
11 that detects a subclass of IgE which is specific for a particular antigen. And
12 that depends upon whether you pull down all the IgE or whether you're only
13 pulling down IgE that binds an antigen.

14 MS. PUGLIELLI: And even then --

15 JUDGE LEOVITZ: But -- but both those embodiments are
16 taught in Johansen. And what Frank is telling you, if you use an Fcε
17 receptor antibody, you get even better results because you don't get cross-
18 reactivity with IgG or any other nonspecific components.

19 That's sort of the prima facie case that the examiner is making.
20 And I don't see how your results show that that prima facie case has a hole in
21 it.

22 MS. PUGLIELLI: Well, the question would be, if one were to
23 take a receptor and put it into the method of Johansen, what would trigger
24 the artisan to make only that substitution and not to substitute any of the
25 other components that are in Frank, too, without having to employ hindsight,

1 looking at the invention and saying, in retrospect, that it would be obvious.

2 And, of course, that would be an inappropriate conclusion to make.

3 JUDGE ADAMS: Okay, well, Franks makes a comparison
4 between anti-FC Ig and using the Fcε receptor, correct?

5 MS. PUGLIELLI: Yes, again, for the purposes of trying to
6 optimize --

7 JUDGE ADAMS: What other reagent is there disclosed in
8 Franks where he distinguishes between some advantage between it and
9 something else?

10 MS. PUGLIELLI: Between?

11 JUDGE ADAMS: You're saying there's no motivation to
12 selectively take Frank's teaching of the advantage of using Fcε receptor over
13 the use of an anti-FC antibody. You're saying that -- that teaching that
14 teaches that advantage, why would one just pick that one and not any other
15 reagent and make that substitution from Franks into Johansen?

16 MS. PUGLIELLI: That --

17 JUDGE ADAMS: My question to you is, what other reagents,
18 other than the Fcε receptor, does Franks teach as having an advantage over
19 something that Johansen used?

20 MS. PUGLIELLI: Well, the -- I mean, the -- Frank focuses
21 mostly on the receptor. But in terms of looking at the invention as a whole,
22 it's not only an issue of using the receptor; it's also an issue of preserving
23 these interactions that happen in vivo between the antibody and the receptor.
24 In addition to preserving interfering interactions that happen. For example,
25 CD21 also has the ability to bind to the low affinity receptor. If CD21 were

1 present in the sample, CD21 could compete for binding with the IgE to that
2 receptor.

3 Interference interactions like that, there is a teaching in Frank
4 that says you certainly could treat the sample to remove those kind of
5 interfering particle. So again, that would demonstrate that what Frank really
6 is going after is, regardless of the discussion of a receptor, is that Frank is
7 going after optimizing detection of IgE and not so much trying to preserve
8 these interactions and these "contaminants" in the sample, if you will, that
9 might interfere with that detection. The invention wants to preserve those
10 things.

11 JUDGE LEBOVITZ: And how does preserving those
12 interactions make it better? I mean, the way I was looking at it, it looked
13 like the preservation of the interactions was only allowing you to capture a
14 particular class of IgE, which was specific for an antigen.

15 MS. PUGLIELLI: Well, it goes beyond that.

16 JUDGE LEBOVITZ: Okay.

17 MS. PUGLIELLI: Because what you were talking about, for
18 example, of using an antibody to just simply capture all IgE and then using
19 an antibody to capture IgE that deals with a specific ligand, or ligand, the
20 invention goes a significant step further in that you're not just asking which
21 of those IgEs bind to a particular Ligand, which of them are present in a
22 sample. You're asking which of them can actually participate in an immune
23 response and therefore which of them are going to be active.

24 For example, I would suggest that a physician who sees a very
25 high level of IgE but knows, because of the results that the invention
26 provides, that a significant percentage of that IgE is inactive is not going to

1 be as concerned with a patient showing that profile as he or she will be with
2 a patient showing a moderate level of IgE. But a high proportion of that
3 being active in an immune response.

4 JUDGE LEBOVITZ: I understand.

5 MS. PUGLIELLI: Now, the other issue as far as the
6 prosecution is concerned is that the examiner really hasn't provided a basis
7 for an expectation of success in making this combination. Most of what we
8 have been talking about, I think, is dealing with the motivation to combine.
9 And, of course, that is another required element of obviousness, that there be
10 an expectation of success.

11 JUDGE ADAMS: So your argument is that the Fcε receptor,
12 one wouldn't expect to be able to bind IgE with the Fcε receptor when it's
13 bound to a solid support? Is that your argument?

14 MS. PUGLIELLI: For which reference in particular?

15 JUDGE ADAMS: The combination of Franks and Johansen.
16 So if we can get past this idea that one would modify Johansen by putting an
17 FC receptor on its -- on its solid base, even if we could get past that, your
18 argument is there's no expectation of success that this FCE receptor would
19 continue to bind IgE?

20 MS. PUGLIELLI: Well, the premise being that again, in vivo,
21 you're not having a receptor sitting immobilized on a platform. These
22 receptors are sitting on cells which, in turn, are in a dynamic state within the
23 host. And again, the invention mimics this.

24 So it's not so much an issue of whether we believe it would
25 work or it wouldn't work. If you use something immobilized to a surface,

1 that removes it from the realm of the invention because you're not
2 mimicking these in vivo interactions.

3 JUDGE ADAMS: Any other arguments with regard to the first
4 obviousness rejection?

5 MS. PUGLIELLI: The combination of Johansen, Frank and
6 Johnson was the first --

7 JUDGE ADAMS: Correct.

8 MS. PUGLIELLI: I'll just try to recount what we've discussed
9 to make sure -- well, the other thing that I would add is that Johnson is only
10 discussing CD23 in -- you know, what the examiner refers to in Johnson is
11 really just an overview of CD23, the fact that it can happen in soluble forms
12 and that the fact that the soluble forms can, in turn, regulate levels of IgE.
13 And that is something very different from employing CD23 in an assay to
14 detect IgE.

15 And the rest of that reference really deals with trying to inhibit
16 the cleavage of CD23 from the surface of a cell and how that would
17 beneficially keep down the levels of IgE. So the type of teaching in
18 Johnson, as far as the background of CD23, I mean, that was discovered in
19 the late '80s, and that kind of background is really known and it doesn't
20 contribute anything of relevance to the context of the invention, aside from
21 just providing a general teaching that one could obtain anywhere, really.

22 JUDGE ADAMS: Did you want to make comments about the
23 combination with Arnold?

24 MS. PUGLIELLI: Yeah, as far as Arnold is concerned, again,
25 it's a similar situation as with Johnson, in the sense that the examiner is
26 pointing to a very general background paragraph that just talks about assays

1 that employ a separation step. And for that matter, it talks about an assay in
2 which you have an antibody that is again immobilized to a surface. It's not
3 talking about receptors at all. It's not talking about detecting IgE at all. And
4 again, there if you look at the entire thrust of the reference, you're talking
5 about a reference that's identifying new types of labels that will change their
6 stability when they are involved in a complex. Basically, you're trying to get
7 rid of separation steps -- that's what Arnold is teaching -- and trying to go
8 more into the realm of a homogenous assay system where you don't have to
9 do these separation steps.

10 Again, that is far removed from the invention. It doesn't
11 mention a receptor at all. And really has no nexus between the other two
12 references, Johansen and Frank. And we've discussed Johansen and Frank
13 together and, again, those fall apart because without hindsight, the skilled
14 artisan would not know to only substitute an FC receptor. The skilled
15 artisan would also potentially substitute many other of the types of reagents
16 that Frank teaches, again, with both Johansen and Frank teaching towards
17 maximizing identification of IGE in a sample, as opposed to doing an assay
18 that's more reflective of what's going on in vivo.

19 JUDGE MILLS: The motivation for making the substitution of
20 the receptor doesn't have to be the same and achieve the same result as the
21 motivation of the appellant in this case, though. The case law is pretty clear
22 on that. So --

23 MS. PUGLIELLI: Well, the fact would still remain, though, in
24 order for you to come up with the invention from Frank 2, and Johansen,
25 you would have to select a specific combination of all of the elements that
26 are taught in Johansen and all of the elements that are taught in Frank 2.

1 And Frank may discuss using a canine FC1 receptor, but it lists
2 all of the other ingredients in its assays. It basically lists many, many, many
3 combinations of different assays that could be run, depending on which
4 component that you linked to what kind of surface, what format is it, is it a
5 radio-immunoassay, is it an Elisa? And it doesn't teach these different
6 components and these different combinations and these different assay
7 formats in a way that points the artisan towards this specific combination.

8 And again, if Frank were to say that using antibodies to do the
9 detection is not the way to go, then without hindsight, what would point the
10 artisan towards Johansen at all in terms of an assay format?

11 But in the absence of hindsight, there's nothing in Frank that is
12 going to point the artisan to using this specific combination. There would be
13 hundreds of thousands of different combinations based on the teaching of
14 Frank in terms of developing different assay formats with different
15 combinations of reagents in order to arrive at something close to the
16 invention.

17 And there's just no -- there's nothing to point the way. They are
18 taught equally in the reference.

19 JUDGE ADAMS: Any other questions?

20 JUDGE MILLS: No, I don't think so.

21 JUDGE ADAMS: Any other questions?

22 JUDGE LEBOVITZ: No.

23 JUDGE ADAMS: Okay, thank you.

24 MS. PUGLIELLI: Thank you very much.

25 (The hearing was concluded at 2:37 p.m.)